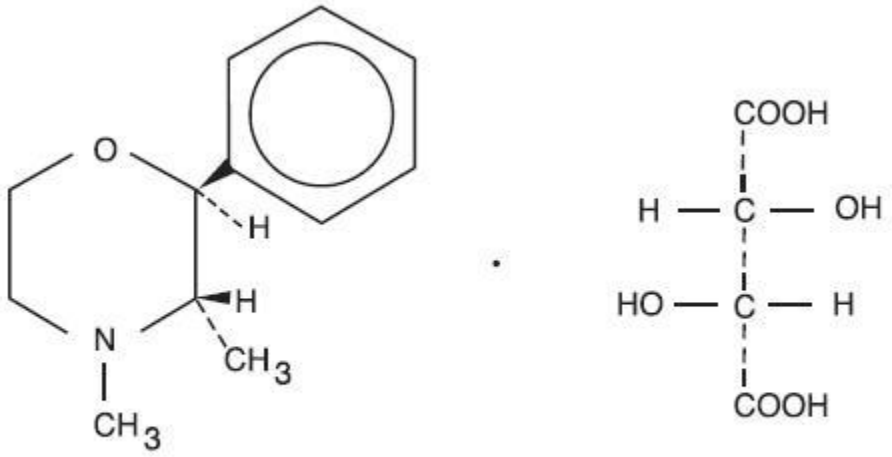
BONTRIL PDM - phendimetrazine tartrate tablet
Valeant Pharmaceuticals, Inc.

DESCRIPTION

Phendimetrazine tartrate, as the dextro isomer, has the chemical name of (2S,3S)-3,4-Dimethyl-2-phenylmorpholine L-(+)- tartrate (1:1).
The structural formula is:



$C_{12}H_{17}NO \cdot C_4H_6O_6$ M.W. 341.36

Phendimetrazine tartrate is a white, odorless cyrstalline powder. It is freely soluble in water; sparingly soluble in warm alcohol, insoluble in chloroform, acetone, ether and benzene.
In addition, the following inactive ingredients are present: Compressible Sugar, Confectioner's Sugar, D&C Yellow #10, FD&C Blue #1, FD&C Yellow #6, Isopropyl Alcohol, Lactose Anhydrous, Magnesium Stearate, Microcrystalline Cellulose, Povidone, Purified Water, Sodium Starch Glycolate.

CLINICAL PHARMACOLOGY

Phendimetrazine tartrate is a sympathomimetic amine with pharmacological activity similar to the prototype drugs of this class used in obesity, the amphetamines. Actions include central nervous system stimulation and elevation of blood pressure. Tachyphylaxis and tolerance have been demonstrated with all drugs of this class in which these phenomena have been looked for.
Drugs of this class used in obesity are commonly known as "anorectics" or "anorexigenics". It has not been established, however, that the action of such drugs in treating obesity is primarily one of appetite suppression. Other central nervous system actions or metabolic effects, may be involved.
Adult obese subjects instructed in dietary management and treated with anorectic drugs, lose more weight on the average than those treated with placebo and diet, as determined in relatively short term clinical trials.
The magnitude of increased weight loss of drug-treated patients over placebo-treated patients is only a fraction of a pound a week. The rate of weight loss is greatest in the first weeks of therapy for both drug and placebo subjects and tends to decrease in succeeding weeks. The possible origin of the increased weight loss due to the various drug effects is not established. The amount of weight loss associated with the use of an anorectic drug varies from trial to trial, and the increased weight loss appears to be related in part to variables other than the drug prescribed, such as the physician investigator, the population treated, and the diet prescribed. Studies do not permit conclusions as to the relative importance of the drug and non-drug factors on weight loss.
The natural history of obesity is measured in years, whereas the studies cited are restricted to a few weeks duration; thus, the total impact of drug-induced weight loss over that of diet alone must be considered clinically limited.

INDICATIONS AND USAGE

Bontril® PDM (phendimetrazine tartrate) is indicated in the management of exogenous obesity as a short term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction. The limited usefulness of agents of this class (see**CLINICAL PHARMACOLOGY**) should be measured against possible risk factors inherent in their use such as those described below.

CONTRAINDICATIONS

Known hypersensitivity or idiosyncratic reactions to sympathomimetics.

Advanced arteriosclerosis, symptomatic cardiovascular disease, moderate and severe hypertension, hyperthyroidism, and glaucoma.
Highly nervous or agitated patients.
Patients with a history of drug abuse.
Patients taking other CNS stimulants, including monoamine oxidase inhibitors.

WARNINGS

Tolerance to the anorectic effect usually develops within a few weeks. When this occurs, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued.
Use of phendimetrazine tartrate within 14 days following the administration of monoamine oxidase inhibitors may result in a hypertensive crisis.
Abrupt cessation of administration following prolonged high dosage results in extreme fatigue and depression. Because of the effect on the central nervous system phendimetrazine tartrate may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly.

PRECAUTIONS

Caution is to be exercised in prescribing phendimetrazine for patients with even mild hypertension.
Insulin requirements in diabetes mellitus may be altered in association with the use of phendimetrazine tartrate and the concomitant dietary regimen.
Phendimetrazine tartrate may decrease the hypotensive effect of guanethidine. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage.
Usage in Pregnancy: Safe use in pregnancy has not been established. Until more information is available, phendimetrazine tartrate should not be taken by women who are or may become pregnant unless, in the opinion of the physician, the potential benefits outweigh the possible hazards.
Usage in Children: Bontril® PDM (phendimetrazine tartrate) is not recommended for use in children under 12 years of age.

ADVERSE REACTIONS

Cardiovascular: Palpitation, tachycardia, elevation of blood pressure.
Central Nervous System: Overstimulation, restlessness, dizziness, insomnia, tremor, headache; rarely psychotic episodes at recommended doses, agitation, flushing, sweating, blurring of vision.
Gastrointestinal: Dryness of the mouth, diarrhea, constipation, nausea, stomach pain.
Genitourinary: Changes in libido, urinary frequency, dysuria.

DRUG ABUSE AND DEPENDENCE

Controlled Substance: Bontril® PDM (phendimetrazine tartrate) is a Schedule lll controlled substance.
Dependence: Phendimetrazine tartrate is related chemically and pharmacologically to the amphetamines. Amphetamines and related stimulant drugs have been extensively abused, and the possibility of abuse of phendimetrazine should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. Abuse of amphetamines and related drugs may be associated with intense psychological dependence and severe social dysfunction.
There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity and personality changes. The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia.

OVERDOSAGE

Acute overdosage with phendimetrazine tartrate may manifest itself by the following signs and symptoms: unusual restlessness, confusion, belligerence, hallucinations, and panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension, or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Poisoning may result in convulsions, coma, and death.
The management of overdosage is largely symptomatic. It includes sedation with a barbiturate. If hypertension is marked, the use of a nitrate or rapid-acting alpha receptor-blocking agent should be considered. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendations for its use.

DOSAGE AND ADMINISTRATION

Usual Adult Dosage: 1 tablet (35 mg) b.i.d. or t.i.d., one hour before meals.
Dosage should be individualized to obtain an adequate response with the lowest effective dosage. In some cases, ½ tablet (17.5 mg) per dose may be adequate. Dosage should not exceed 2 tablets t.i.d.

HOW SUPPLIED

Three-layered green, white and yellow tablet with “B 35” on the scored side and the letter “V” on the other. Bontril® PDM tablets containing 35 mg of phendimetrazine tartrate are available in bottles of 100 (NDC 0187-0497-01) and 1000 (NDC 0187-0497-02).

Store at 25°C (77°F); excursions permitted to 15°C-30°C (59°F-86°F).
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